

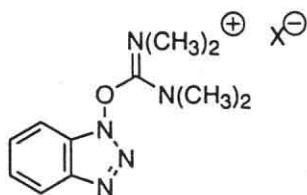
Prof. C. McKenna Chem 519 Le Big Problem Set

Feb. 14, 2003

Total: 140 Pts.
[11AM]

Due: Feb. 24, 2001

1. (20) Devise a solid-phase peptide synthesis scheme, starting from unprotected amino acids, for: ADCKR. You can either devise your own or use literature references. Annotate each step explaining your reasoning for reagents & conditions used.
2. (20) A peptide has the sequence KEYS-SCIENCE.
(a) Show all species present during a titration with NaOH from pH 2-14.
(b) Estimate the pI.
3. (20) A synthesis of amino acids published in 1892 (Azlacton Synthesis) converts N-Ac-Glycine by reaction with Ac_2O ; $\text{NaOAc}/\text{R}'\text{CHO}$; H_2/Pd ; HCl to $\text{R}'\text{CH}_2(\text{NH}_3)(\text{CO}_2\text{H})^+ \text{Cl}^-$.
(a) Write a mechanism.
(b) This method gives racemic amino acids. In class we referred to the oxazolone mechanism of racemization. Give the latter and compare to your result in (a).
4. (20) Locate a protein database and retrieve data for normal human Mb-O₂. Use Chime or Rasmol to construct the 3D structure. Show all work. Based on the structure (included in your answer), characterize
(a) the heme pocket along the protoporphyrin periphery;
(b) is there a difference between the pocket environments on the oxygen-binding and opposite faces of the heme? Comment.



5. (20) The reagent shown promotes coupling of RCO_2H with $\text{R}'\text{NH}_2$ to form an amide RCONHR' . Write a mechanism, explaining your reasoning. Name of reagent?

6. (20) PGH2-synthase mediates prostaglandin synthesis and is inhibited by the anti-inflammatory and analgesic, ibuprofen. Given the data, find K_m , V_m for the enzyme, then K_i for the inhibitor and explain what type of inhibition is involved. Calculate the turnover number and time required for one catalytic reaction. Data: $e_0 = 3 \text{ mg/mL}$; $\text{MW} = 61\text{K daltons}$; $[I] = 0.3 \text{ mM}$;

Substrate mM	V mM/min	V + Inh mM/min
.5	23.5	16.67
1	32.2	25.25
1.5	26.9	30.49
2.5	41.8	37.04
3.5	44	38.91

7. (20)

- Find the number of possible SS bonds in a protein containing 20 Cys (Ok to derive a general solution, or else give the actual number.)
- Calculate the volume of 0.025 M HEPES buffer required to exchange a protein solution (20 mL) that is 0.1 M in TRIS to 0.025 M HEPES and $< 0.001 \text{ M}$ TRIS by diafiltration, showing all work.